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Office of Surveillance and Epidemiology**

Drug Use Review

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Drug Name(s): Ofirmev™ (Acetaminophen) Solution for Infusion

Application Type/Number: NDA 022450

Applicant/sponsor: Cadence Pharms

OSE RCM #: 2012-1016

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EXECUTIVE SUMMARY

The Office of Pediatric Therapeutics (OPT) and Pediatric and Maternal Health Staff (PMHS) requested an analysis of the drug utilization patterns for Ofirmev™ (acetaminophen solution for infusion). As a result, this review analyzes the drug utilization patterns of Ofirmev™ in the patient populations aged 0-1, 2-16 and 17+ years from non-federal hospitals from product approval (November 2011) through February 2012.

Discharge and patient counts from the non-federal hospital settings:

- Approximately 76,800 discharges and 74,900 patients were associated with a hospital billing for Ofirmev™ over the cumulative time period from November 2010 through February 2012.
- The majority of Ofirmev™ use was among patients aged 17 years and older, accounting for 98.5% of total patients.
- Patients aged 2-16 years old accounted for around 1.5% of total patients associated with a hospital billing for Ofirmev™.
- Patients aged 0-1 years old accounted for far less than 1% of total patients associated with a hospital billing for Ofirmev™.

1 INTRODUCTION

In preparation for the Pediatric Advisory Committee meeting in September 2012, the Office of Pediatric Therapeutics (OPT) and Pediatric and Maternal Health Staff (PMHS) requested a review of the drug utilization patterns for Ofirmev™. Using the currently available proprietary drug use databases, this review summarizes the drug utilization patterns in terms of discharges and patients with a hospital billing for Ofirmev™, stratified by patient age (0-1, 2-16 and 17+ years), from non-federal hospitals from November 2010 through February 2012, cumulative.

2 BACKGROUND

2.1 REGULATORY HISTORY

Ofirmev™ was approved on November 2, 2010, under NDA 022450 for the management of mild to moderate pain, the management of moderate to severe pain with adjunctive opioid analgesics, and the reduction of fever. It was approved for use in patients aged 2 years and older.¹

2.2 PRODUCT LABELING

Ofirmev™ is supplied as a solution for infusion with a concentration of 1000 milligrams per 100 milliliters (10mg/ml).

3 METHODS AND MATERIAL

¹ U.S. Food and Drug Administration: Drugs@FDA. Ofirmev™ Approval History. Accessed in May 2012. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#labelinfo

3.1 DETERMINING SETTINGS OF CARE

The IMS Health, IMS National Sales Perspectives™ (see Appendix 1 for full database description) was used to determine the various retail and non-retail channels of distribution for Ofirmev™. Over the cumulative time period from November 2010 through February 2012, sales data indicated that nearly 100% of Ofirmev™ vials were sold to non-retail settings (non-federal hospitals, home healthcare, federal facilities, clinics, long-term care, prisons, universities, etc.). Of these, non-federal hospitals accounted for approximately 91% of Ofirmev™ sales in the non-retail settings.² As a result, non-federal hospital utilization patterns were examined. Mail order and outpatient retail settings data were not included in this analysis.

3.2 DATA SOURCES USED

Proprietary drug use databases were used to conduct this analysis (see Appendix 1 for full databases description).

The IMS Health, Inpatient Healthcare Utilization System (IHCARUS) database was used to obtain the estimated number of discharges and patients associated with a hospital billing for Ofirmev™, stratified by patient age (0-1, 2-16, and 17+ years), from the inpatient and outpatient ER settings of non-federal hospitals from November 2010 through February 2012, cumulative.

4 RESULTS

4.1 NUMBER OF DISCHARGES AND PATIENTS WITH A HOSPITAL BILLING FOR OFIRMEV™

Table 1 provides the nationally estimated number of discharges and patients associated with a hospital billing for Ofirmev™ from the U.S. non-federal hospitals. Over the cumulative time period from November 2010 through February 2012, approximately 76,800 discharges and 74,900 patients were associated with a hospital billing for Ofirmev™. Of these, the majority of Ofirmev™ use was among discharges and patients aged 17 years and older, accounting for around 98.5% each of total discharges and total patients. Discharges and patients aged 2-16 years old accounted for approximately 1.5% each of total discharges and total patients. Far less than 1% each of total discharges and total patients with a billing for Ofirmev™ were ages 0-1 years.

Table 1. Nationally estimated number of discharges and patients associated with a hospital billing for Ofirmev™ from the U.S. non-federal hospitals, cumulative November 2010 through February 2012

	Cumulative 11/2010-2/2012			
	Discharges	%	Patients	%
Total Ofirmev™	76,756	100.0%	74,935	100.0%
0 - 1 years	33	0.0%	33	0.0%
2 - 16 years	1,119	1.5%	1,119	1.5%
17+ years	75,596	98.5%	73,775	98.5%
Unknown Age	7	0.0%	7	0.0%

Source: IMS Health, Inpatient Healthcare Utilization System. November 2010 through February 2012. Data extracted May 2012. File: IHCARUS 2012-1016 Ofirmev (APAP) age form 5-18-12.xls

² Source: IMS Health, IMS National Sales Perspectives™, November 2010 to February 2012. Data extracted April 2012. File: NSPC 2012-1016 Ofirmev (APAP) channels 4-11-12.xls

5 LIMITATIONS

Findings from this review should be interpreted in the context of the known limitations of the databases used. Based on the IMS Health, IMS National Sales Perspectives™, sales data showed that the majority of Ofirmev™ was sold to non-retail settings, mainly non-federal hospitals, over the cumulative time period from November 2010 through February 2012. These data do not provide a direct estimate of use but do provide a national estimate of units sold from the manufacturer to various channels of distribution. The amount of product purchased by these retail and non-retail channels of distribution may be a possible surrogate for use, if we assume that facilities purchase drugs in quantities reflective of actual patient use.

The IMS inpatient charge data master (CDM) sample does not include Federal hospitals, including VA facilities, and some other specialty hospitals, and does not necessarily represent all acute care hospitals in the U.S. in all markets. Caveats of the IMS inpatient data source are common to this type of charge information, but are mostly limited to limitations of charge descriptions and what is actually entered by the sample hospitals. However, validations of the IMS CDM data using both the National Hospital Discharge Survey (NHDS) and the AHRQ HCUP data have shown IMS's data to be accurate across many therapeutic areas. We are continuing to explore other data sources which will allow more rigorous statistical analysis of trends over time, including the calculation of rates and confidence intervals. Due to the limitation of the databases available to the Agency, data on prescribing specialty and diagnoses associated with use of Ofirmev™ are not available.

We focused our analyses on only the non-federal hospital settings, therefore these estimates may not apply to other settings of care in which these products are used (e.g., retail and mail order settings). The estimates provided are national estimates, but no statistical tests were performed to determine statistically significant changes between products. Therefore, all changes between products should be considered approximate, and may be due to random error.

6 CONCLUSIONS

There were approximately 76,800 discharges and 74,900 patients associated with a hospital billing for Ofirmev™ over the time period examined. Off-label use of Ofirmev™ in patients aged 0-1 years old appeared negligible.

APPENDIX 1: DATABASES DESCRIPTION

IMS Health, IMS National Sales Perspectives™: Retail and Non-Retail

The IMS Health, IMS National Sales Perspectives™ measures the volume of drug products, both prescription and over-the-counter, and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. Volume is expressed in terms of sales dollars, eaches, extended units, and share of market. These data are based on national projections. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, food stores, and mail service. Outlets within the non-retail market include clinics, non-federal hospitals, federal facilities, HMOs, long-term care facilities, home health care, and other miscellaneous settings.

IMS Health, Inpatient HealthCare Utilization System (IHCareUS)

The IMS, Inpatient HealthCare Utilization System (IHCareUS) provides hospital inpatient and outpatient emergency department encounter transactions and patient level data drawn from hospital operational files and other reference sources. Encounter information is available from mid-2001, are collected weekly and monthly and are available 25-30 days after the end of each monthly period. This robust data set includes > 650 hospitals with hospital inpatient and outpatient encounter data linked to each appropriate patient as well as to select individual hospital departments by anonymized, consistent, longitudinal patient identifiers. These data include >7 million annual hospital inpatient encounters and >60 million annual hospital outpatient encounters (including ED visits) representing acute care, short-term hospital inpatient sites, and their associated hospital emergency departments in order to measure and track the near term health care utilization of hospitalized patients. Each hospital patient encounter includes detailed drug, procedure, device, diagnosis, and applied charges data as well as location of initiation of each service within the hospital setting of care (e.g. Pediatric, ICU) by day for each patient's entire stay, as well as patient demographics and admission/discharge characteristics. IMS' datasets are geographically representative, and include claims across all third-party payer types, including commercial insurers, Medicare, Medicare Part D, Medicaid and other payer types.

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/s/

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06/18/2012

Drug use data were cleared for public release.

HINA S MEHTA

06/18/2012

Drug use data cleared

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06/18/2012